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Cardiac Hypert
and
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THE RELATIONS

OF

CARDIAC HYPERTROPHY

TO

RENAL DISEASE.

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THE RELATIONS OF CARDIAC HYPERTROPHY TO RENAL DISEASE.

THE coincidence of cardiac hypertrophy with renal disease, more especially with granular degeneration of the kidneys, is so frequent, and so often wanting in any local mechanical explanation, that it has always attracted considerable attention, and, although the discussion has not yet arrived at a very definite settlement of the question, it has been the cause of a thorough examination of the entire pathological relations of Bright's disease, which has produced results of the highest practical importance.

The frequency of this coincidence seems to be in about one-half of the cases. It cannot be admitted that its absence is due to the renal disease being not far enough advanced. Doubtless the coincidence would be very much more complete were all the cases of hypertrophy included in the statistics, but those explicable by valvular or vascular disease have been excluded. Some authorities give a much larger proportion than one-half, and, perhaps, it is difficult to determine who is right; but this we do know, that the heart is not always hypertrophied even when the kidneys are very contracted. In

the other forms of Bright's disease, hypertrophy, though common, is certainly less frequent.

Bright,* in recording the various organic changes in 100 cases of renal disease, says, "The obvious structural changes in the heart have consisted chiefly of hypertrophy, with or without valvular disease; and what is most striking, out of fifty-two cases of hypertrophy, no valvular disease whatsoever could be detected in thirty-four; but in eleven of these thirty-four, more or less disease existed in the coats of the aorta; still, however, leaving twenty-two without any probable organic cause for the marked hypertrophy generally affecting the left ventricle. This naturally leads us to look for some less local cause for the unusual efforts to which the heart has been impelled; and the two most ready solutions appear to be, either that the altered quality of the blood affords irregular and unwonted stimulus to the organ immediately, or, that it so affects the minute and capillary circulation as to render greater action necessary to force the blood through the distant sub-divisions of the vascular system." In the next paragraph, he says, "It is observable that the hypertrophy of the heart seems, in some degree, to have kept pace with the advance of disease in the kidneys; for in the majority of cases where the muscular power of the heart was increased, the hardness and contraction of the kidney bespoke the probability of a long continuance of the disease."

In this table Bright had included not only granular kidney, but all forms of renal disease with albuminuria. It will be found that the pendulum of modern opinion is now again oscillating between these two explanations in spite of forty years of discussion and observation with

* Cases of Renal Disease accompanied with Albuminous Urine. Guy's Hospital Reports, vol. i., p. 397.

the aid which the modern use of the microscope has lent to pathological researches. Thus Prof. Senator,* of Berlin, in a recent communication suggests that in chronic parenchymatous nephritis the heart is excentrically hypertrophied, and that this is probably attributable to the increased capillary resistance while, in interstitial nephritis, the hypertrophy is concentric, and is due to direct irritation of the heart, either from some nervous disorder, as in Basedow's disease, or, as is more likely, from the blood dyscrasia.

Since the time of Bright there have been four original explanations brought forward and all other writers on the subject have adopted some one, or a combination, of these various theories.

Traube, to whom we owe the observation of the hard pulse of Bright's disease, regarded the destruction of a large capillary area in the kidneys as necessarily causing so much obstruction to the circulation that, aided by the imperfect elimination of water, the blood pressure in the aortic system must rise and cardiac hypertrophy follow. Bamberger objected to this that the hypertrophy begins in the earlier stages of Bright's disease; moreover it is present in chronic parenchymatous nephritis in which no destruction of capillaries has occurred. Ludwig and his pupils have shown that ligature of both renal arteries, or of even larger arteries, does not raise the blood pressure in the aorta, while it is well known that in granular kidney the elimination of water is rather in excess of the normal yet it is specially in this affection that cardiac hypertrophy occurs. It is, therefore, not without reason that this hypothesis has been generally abandoned,

* Beitrage zur Pathologie der Nieren und des Harns. Ueber die Beziehungen der Herzhypertrophie zu Nierenleiden. Virchow's Archiv. Bd. 4. lxxiii. Heft 3, p. 313.

although in recent times it received the support of so eminent an authority as Bartels.

The next original explanation was that given by Dr. George Johnson, which has undergone at least two modifications. In the first place Dr. Johnson pointed out the excessive thickening of the muscular walls of the renal arterioles, and suggested that the obstruction to the circulation offered by a state of tonic spasm in these vessels, would explain their own alterations, the rise of blood pressure and the cardiac hypertrophy. But having been able to discover similar changes in the vessels of the pia mater and mesentery, he enlarged his hypothesis and imagined a state of tonic spasm of the whole systemic arterioles which he attributed at first to direct irritation by the impure blood, and later on to stimulation of the vaso-motor centre. According to his present views he regards the condition as analogous to asphyxia, in which unoxygenated blood going to the brain stimulates the vaso-motor centre in the medulla, and causes contraction of the arterioles throughout the body with consequent increase of the arterial blood pressure. The great objection to this theory of general constriction of the vascular system is that, under such circumstances, the urinary secretion would be diminished or suppressed, as indeed occurs in asphyxia ; whereas, in granular kidney, as is well known, the rise in blood pressure is accompanied by an increase in the flow of urine. Moreover, Grutzner (Pflüger's Archiv Bd. xi., s. 370) has shown that the diuresis excited by the intravascular injection of salts such as nitrate of potash is arrested during suspension of the respiration, unless the nerves to the kidney are divided. This failure in the analogy has always appeared to us a very weak point in the theory, but recently further light

has been thrown on the question. MM. Dastre and Moret* have communicated to the Société de Biologie the results of their investigations into the state of the circulation in asphyxia. They have determined that the vessels of the skin in an asphyxiated animal are dilated to five or ten times their normal diameters, but that the vessels of the intestines and viscera are at the same time contracted, this antagonism holding good in the reverse condition, when the skin vessels are contracted those of the internal organs are dilated.

As the depression of the cutaneous circulation and functions are as prominent features of granular kidney as the increase in the renal secretion, it seems probable that if any vaso-motor action does occur it must be contraction of the vessels of the skin and dilatation of the vessels of the internal organs. Under such circumstances this vaso-motor action may play some part in the rise of blood pressure.

The third original explanation is that which we owe to Sir William Gull and Dr. Sutton.† They rediscovered the vascular changes described by Dr. Johnson, but drew attention more especially to the thickening of the fibroid tissues. They regard these vascular changes as primary and essential, the increased blood pressure and cardiac hypertrophy being their consequences while the kidney disease is but a local expression of a general degeneration of the arterioles and capillaries attended by atrophy of the adjacent tissues. Although we may admit that when established these vascular changes do obstruct the circulation, and thus might be determining causes of cardiac hypertrophy, according to Thoma‡ the fibroid thickening occurs

* Influence du Sang Asphyxique sur la Circulation. Société de Biologie. Séance du 8 Novembre. Le Progrès Médical, Nov. 15th

† Medico-Chir. Trans. Second Series. Vol. xxxvii., p. 273.

‡ Zur Kentniss der Circulationsstörung in der Nieren bei chronischer interstitieller Nephritis. Virchow's Archiv Bd. lxxi. Heft 1 & 2.

in *dilated* vessels so that the normal calibre is only exceptionally reduced. But in addition we have the fact that in a considerable proportion of cases of granular kidney cardiac hypertrophy is found unaccompanied by the vascular changes. According to Ewald* this occurred in 4 out of 20 cases, and we have been able to confirm the statement in about the same proportion of cases (2 out 10). Finally in chronic parenchymatous nephritis the occurrence of cardiac hypertrophy is not infrequent, but the vascular changes are quite exceptional. Therefore, although there is much in the view taken of Bright's disease by these authors with which we cordially agree, we must regard their explanation of the cardiac hypertrophy as failing to square with all the facts of the case.

The latest explanation we owe to v. Buhl.† He believes the cardiac and renal changes proceed *pari passu*, the hypertrophy is to be attributed to the self-increased activity (Selbsteigene Thatigkeit) of the heart. Myocarditis occurs very early, which may cause no alteration, or atrophy or hypertrophy of the organ. Most frequently it causes hypertrophy. As the inflammatory process comes to an end the cardiac muscle hypertrophies from excess of nutrition, and to overcome the increased work of the dilated ventricle. In addition he regards the fact as 'quite new,' that a relative stenosis of the aorta is present. The rise of blood pressure in the aortic system is due to the hypertrophy of the ventricle and the narrowing of the aorta.

The relative frequency of myocarditis in renal disease is an undoubted fact, and this process plays an important

* Ueber die Verauderungen kleiner Gefasse bei Morbus Brightii und die darauf Bezuglichlen Theorien. Virchow's Archiv Bd. lxxi. Heft 4.

† Ueber Bright's Granularschwund der Nieren und die damit zusammenhängende Herzhypertrophie. Mittheilungen aus dem pathol. Institut zu München, 1878. S. 38.

part in many cases, but there is no warrant in the assumption that it has occurred in all cases. Buhl is not at all clear as to the cause upon which the self increased activity of the heart or the myocarditis depends. He cannot claim novelty for the fact that the aorta is in some cases relatively stenosed as Bamberger* adduced it as opposed to Traube's hypothesis. With regard to its frequency in granular kidney Ewald has measured the circumference of the aorta above the valves in 12 cases, and found it to vary between 12.1 and 5.7 cm., the average being 7.6 cm., while the normal circumference according to Bouillaud is 6.3 cm., so that we cannot attach very much importance to it as a cause of cardiac hypertrophy.

Having failed to find any of these explanations quite satisfactory we return to Bright's suggestions, that either the altered quality of the blood affords irregular and unwonted stimulus to the heart immediately; or that it so affects the capillary circulation as to render greater action necessary to force the blood through the distant subdivisions of the vascular system. Both these explanations rest upon the supposed impure state of the blood. In the acute and chronic stages of parenchymatous nephritis the condition of the blood was investigated many years ago by Bostock, Gregory, and Christison.† According to the latter, urea was always found in considerable quantity in the blood whenever the excretion of urine was diminished, the density of the blood serum was always less, and the fibrine was frequently increased. Nothing of importance has been added to this observation in modern times; but experiments with animals have shown that urea, extractive matters of the blood, creatine and leucin, accumulate in large quantities

* Quoted by Niemeyer. Text Book of Practical Medicine. Vol. 1., p. 300.

† Granular Degeneration of the Kidney. 1839. P. 58 et seq.

in the blood and tissues after nephrotomy; and it does not require much argument to convince anyone that during the abeyance of the renal function the blood depurating process must be more or less incomplete.

But in granular kidney, as we understand it, the density of the serum is normal, or increased, according to Christison; the proportion of salts and albumen may be very high, and the fibrine is normal; the most striking characteristic being a rapid reduction of the blood pigment or hæmatin. Bartels has published some observations, but none of them bearing on the state of the blood in the earlier stages; in the latter stages, when dropsy was present, the density of the blood serum was low; a certain amount of urea was found in many cases, in others it was absent.

But there are other reasons for believing that blood impurities are early and important phenomena in granular kidney. Dr. Todd first pointed out the frequent co-existence of this form of renal disease with gout, hence the name Gouty Kidney; Ollivier has drawn attention to its frequent occurrence among workers in lead. Dr. Johnson states that the disease is common in persons who "eat and drink to excess, or who, not being intemperate in food or drink suffer from certain forms of dyspepsia, without the complication of gouty paroxysms." He says, that "renal degeneration is probably a consequence of the long-continued elimination of products of faulty digestion through the kidneys." The late Dr. Murchison was persuaded of the relation borne by contracted kidney to persistent lithæmia. Prof. Semmola,* of Naples, maintains the view that Bright's disease is a consequence of the blood dyscrasia

* Brit. Med. Journal, 1879, II., p., 501. Report of Sixth Amsterdam International Congress of Medical Science.

resulting from suppression of the respiratory function of the skin. Our own observations indicate the probability that prolonged and habitual dyspepsia is in many cases a precursor of this disease.

Therefore, although during the greater part of its course this affection does not lead to any diminution of the renal secretion, there is ground for believing in a blood dyscrasia depending upon other causes.

The next point for enquiry is whether such blood impurity as may arise from defective elimination or perverted digestive functions can be shown under any conditions to obstruct the capillary circulation. Heidenhain* speaks of copious diuresis occurring after the injection of urea *in spite of the blood pressure remaining below normal, or not being proportionately increased.*

Ustimowitsch and Grutzner† determined a certain constant rise in blood pressure after injecting urea into the blood accompanied by increased flow of urine.

Dr. Rendu‡ in his inaugural thesis quotes M. Potain as having noticed that although injections of urea into the blood do not modify the mechanical conditions of the circulation, yet if a mixture of urea and blood serum be allowed to stand some hours, and be then injected, the arterial tension rises to an unexpected degree.

Drs. Paul Grawitz and Oscar Israel‖ found that neither unilateral artificial nephritis nor extirpation of one kidney, although followed by hypertrophy of the heart, effected any rise in the blood pressure. Their experi-

* Pflüger's Archiv, IX., p. i., quoted by Foster. Text book of Physiology, p. 283.

† Quoted by Ewald. Op. cit.

‡ Quoted by Hanot. Contribution à l'étude de l'hypertrophie concentrique du ventricule gauche dans la nephrite interstitielle. Arch. Gen. de Med. 1878, p. 172.

‖ Experimentelle Untersuchungen über den Zusammenhang Zwischen Nierenkrankung und Herzhypertrophie. Virchow's Archiv. Bd. lxxvii., s. 315.

ments are so interesting in relation to the present enquiry, that a further account of them is necessary. By taking strict antiseptic precautions they were able to clamp either of the renal arteries of a rabbit without any unfavourable surgical result. One and a half to two hours afterwards the clamp was removed. In half an hour after the operation the urine became bloody, and, in from one to two hours the organ if examined was found to be grayish red and opaque. If the clamp was allowed to remain on longer the kidney became of a dirty yellowish grey colour, indicating commencing gangrene. The effect of this operation was to cause intense acute parenchymatous nephritis with fatty degeneration of the epithelium of the tubules. This passed into either granular atrophy or the large white kidney. In the former, microscopical examination showed no trace of nuclear prolification, the substance of the organ consisting simply of wasted tubules. In another series of experiments they extirpated one kidney altogether. They found that the results of these conditions varied accordingly as the animals operated on were young and growing, or old, strong, and fully grown.

In the young, after 2 or 3 days, the intact kidney began to increase in size to 20 or 30 per cent. more than its normal weight. As the contraction of the other kidney went on the intact organ continued to increase until it equalled the weight of the two kidneys of an animal of the same size. At the same time they ascertained by abdominal section that the other kidney still secreted a watery urine of low specific gravity, but in small quantity.

In the old animals the intact kidney also increased a little, the greatest being in one case of nephrotomy, where the extirpated right kidney weighed 7.7 grms., and the left, after 82 days, weighed 11.3 grms. The hypertrophy of the kidney consisted in a true hyperplasia of the renal

elements, at least the enlargement was certainly not due to increase in the diameters of the tubules. The consequence of the imperfect compensation by hypertrophy of the other kidney caused in some cases death by acute or chronic uræmia, in others the animals continued to live, but were ill nourished until the deficit was covered by hypertrophy of the left ventricle. By careful estimations of the relative normal weights of the heart and kidneys, and comparison of these data with the weights of the altered organs, they were able to determine that the cardiac hypertrophy bore a definite proportion to the loss of renal substance, and therefore was truly compensatory for the renal defect. As a rule the heart was not dilated, in many the ventricle was in a state of spasmodic contraction, and they were unable to obtain any confirmation of Senator's views already quoted relative to the pathogenesis of excentric and concentric hypertrophy. In those cases where cardiac dilatation occurred, the symptoms during life indicated a primarily defective or later destroyed compensation, the animals died with acute or chronic dropsy, and the weight proved imperfect compensation. In the case of a large black doe, which died with dropsy of all the serous cavities 10 days after the operation, the cardiac muscle was intensely granular, even after the addition of soda solution. They regard this as evidence of the occasional occurrence of *primary* myocarditis. Much more frequently the myocarditis was secondary, but whichever it was it produced the appearance of "excentric hypertrophy." They were never able to obtain evidence of any increased blood pressure, but by careful measurements they determined a constant increase in the velocity of the circulation. Injections of urea also failed to produce a rise of blood pressure, but *stimulated the heart's* action and quickened the blood stream.

Here we have the explanation of the "self increased activity" of the heart, to which Buhl refers, and also of the myocarditis. The impure state of the blood acts as Bright suggested, by affording an unwonted stimulus to the heart immediately, and this leads to a hypertrophy proportionately compensatory for the loss of renal secreting substance. Myocarditis is the cause of dilatation and the subsequent hypertrophy takes place as Buhl indicates from over nutrition, and increased work from the greater capacity of the ventricle. The rise in blood pressure is not a cause of the cardiac hypertrophy; moreover, in these experiments neither the state of the heart, nor the renal condition nor the blood impurity combined, were able to effect any increase in the tension of the aortic system.

But the high pressure pulse of Bright's disease is a constant and now universally admitted fact. Traube asserted, not without reason, that he could diagnose granular kidney by the pulse alone, and Galabin* has shown that the same condition is present in the other forms of Bright's disease. But a great step was taken when Mahomed † proved that this rise in the blood pressure precedes the occurrence of albuminuria, the development of which he watched at the termination of scarlatina. Here there is no question of structural change in the heart or arterioles, the sole condition present is that of faulty elimination due to the morbid state of the skin. When to this constipation is added, the blood pressure rises, blood crystalloids appear in the urine, and if not averted by a sharp purge, albuminuria follows. Moreover, Dr. Mahomed ‡ has recorded cases of high arterial

* On the Connection of Bright's Disease with changes in the Vascular System.

† The Etiology of Bright's Disease and the pre-albuminuric Stage. Med. Chir. Trans. Second Series. Vol. xxxix., p. 197.

‡ Clinical Aspects of Chronic Bright's Disease. Guy's Hosp. Reports, vol. xxiv.

tension, sometimes accompanied by albuminuria in young dyspeptic patients free from cardiac hypertrophy; and we have published similar cases.* In both, it is suggested that in these young persons, we may have to do with the condition which gives rise to granular kidney later in life. In this place it is of interest to quote the following passage from Dr. Murchison's Cronian lectures on "Functional derangements of the liver." He says, "so often have I observed albuminuria associated with hepatic disorder, which has disappeared completely and permanently when this has been set to rights, that I have little doubt that we have in the liver a cause of albuminuria to which attention has not hitherto been sufficiently directed. The pathology of the albuminuria in these cases may be similar to that of certain cases of diabetes already referred to, the liver having too much work to do, and permitting some albumen to pass through in a form which cannot be assimilated; or possibly there may be some defect in the destructive functions of the liver in consequence of which the albuminous matter, instead of being converted into urea, does not even reach the stage of lithic acid. *It is possible that in many of the cases now referred to the albuminuria may indicate an early stage, not yet described, of the contracted or gouty kidney, yet it is certain that the symptoms may persist or recur during many years without any other symptom of renal disease, and with but little impairment of the general health.*" It is especially to the latter part of this passage, which we print in italics, that attention is directed. When we recall the known connection between persistent lithæmia and contracted kidney, and recollect that in these cases we find high arterial tension, retinal hæmorrhages, occasional hyaline casts, albuminuria, and

* The Functional Stage of Granular Kidney. Birm. Med. Rev., Oct., 1879.

lithuria, there is warrant for believing that such an early stage of granular kidney, as Murchison here alluded to, has been recognised clinically.

To return to the matter in hand, if the rise in pressure precedes all structural change it must be due to increased energy in the cardiac contractions, or to obstruction in the distant parts of the vascular system, or to both combined. Most modern writers, Grainger Stewart, Broadbent, Mahomed, Ewald, and others, regard the obstruction as seated in the capillaries, and the cardiac hypertrophy as the consequence of this impediment to the circulation. But we have seen that the cardiac hypertrophy must be regarded as directly dependent on the state of the blood, and therefore is rather to be regarded as a cause than an effect of the rise in blood pressure.

But Israel and Grawitz appear to have proved that the cardiac hypertrophy *per se* does not raise the blood pressure, nor does the state of the blood which manifests itself by the stimulus to the heart's action seem to suffice to produce any peripheral obstruction great enough to cause this result. We are compelled therefore to seek some other factor, or to believe that in some respect the conditions of these experiments differ from those of patients suffering from Bright's disease. Such a difference plainly existed in the intact state of one kidney, and it may be that the increased functional activity of the heart in these animals sufficed to maintain elimination; the rise of blood pressure, with which we are clinically familiar, being the result of a higher degree of toxæmia than that present in these experiments.

As the rise in blood pressure precedes all structural changes, and as the theory of vaso-motor action is inconsistent with the augmented secretion of urine, we may

assume an increase in the capillary resistance as the other factor, which, combined with the augmented cardiac energy, determines the characteristic pulse of Bright's disease. How far Dr. Johnson's theory, modified in accordance with Dastre and Moret's observations, may be accepted as assisting the above named factors, we can not determine, but we are unwilling to exclude it altogether from some share in this partnership, in which one other participator has only a hypothetical existence.

These conclusions, which have been arrived at by combining and comparing pathological, clinical, and experimental data, suggest certain practical conclusions.

1. In chronic Bright's disease the augmentation of the cardiac function is compensatory to the renal defect. This view confirms the propriety of the practice of administering digitalis in these cases. But as far as possible, elimination should be favoured by the skin and bowels, while the diet should consist of elements containing as small an amount of urea-forming substances as the general condition of the patient may warrant.

2. The high tension pulse indicates a high degree of toxæmia and relative failure of the kidneys. As the toxic material in the blood stimulates the heart (Israel and Grawitz) and probably the kidneys (Heidenhain.) without raising the blood pressure, polyuria or even albuminuria may precede any change in the state of the pulse. Careful examination of the urine is therefore of the greatest importance for detecting the earlier stages of the condition which leads to granular degeneration of the kidneys.

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The relations of cardiac hypertrophy to renal disease.